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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/426,792	10/22/1999	DENNIS T. MANGANO	9114-004-999	2354

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EXAMINER
SPIVACK, PHYLLIS G

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 07/12/2002 20

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/426,792	Mangano
Examiner	**Art Unit**
Phyllis Spivack	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 8, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-16, 49-51, and 53-55* is/are pending in the application.

4a) Of the above, claim(s) *7-12* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6, 13-16, 49-51, and 53-55* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's Request for Continued Examination (RCE) filed December 3, 2001, Paper No. 15, is acknowledged. An Amendment filed July 5, 2001, Paper No. 12, is further acknowledged in which new claims 53-55 are presented. The new claims have been renumbered under Rule 126. Claims 1-16, 49-51 and 53-55 are now under consideration.

In response to a Restriction Requirement, Applicants elected Group I, directed to administration of cardiovascular agents that are β_1-adrenergic selective blockers to reduce cardiovascular disease complications following surgery under defined conditions, in Paper No, 19 filed April 8, 2002. Claims 7-12 are withdrawn from consideration by the Examiner, 37 CFR 1.142(b), as directed to non-elected inventions. Re-affirmation of the election is requested when Applicant responds to this Office Action. Claims 1-6, 13-16, 49-51 and 53-55, directed to β_1-adrenergic blockers, are presently under consideration.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 13-16 and 49-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldstein et al., J. Cardiovasc. Pharmacology., particularly in view of Kataria et al., J. Cardiothoracic Anest.

Goldstein teaches the administration of a therapeutic dose of the β1-selective blocking agent atenolol to patients immediately following cardiac-related surgery. Atenolol decreased both heart rate and blood pressure. No patient with bronchospasm, bradycardia, atrioventricular conduction defects, heart failure or recent myocardial infarction was included. See lines 4-10, column 2, page 254. As required by claims 15 and 16, patients suffering from coronary artery disease and those at risk for coronary artery disease were included. Although Goldstein's patient population all underwent coronary artery bypass, the parameters following atenolol administration are also monitored in non-cardiac related surgery. See Figures 1-3. See Table 2 where the heart rate before atenolol administration is 90.3 +/- 3.3, which meets the requirement of "greater than or equal to 65 bpm" in claims 1 and 49. Kataria teaches the administration of another β_1-adrenergic clocking agent, esmolol, immediately after general surgery, during emergence from anesthesia, to reduce cardiovascular disease complications. Bronchospasm and congestive heart failure are not observed. Doses ranging from 100 to 2,104 mg of esmolol were given. This dosage range would reasonably meet the limitation in claims 1 and 49 "near the maximum effective dose". Accordingly, one skilled in the cardiology art would have been motivated to administer a β_1-selective blocking agent to reduce cardiovascular complications following surgery in view of the combined teachings of Goldstein and Kataria. Such would have been obvious in the absence of evidence to the contrary because a heart rate at or slightly above 65 bpm and a systolic blood pressure reading slightly over 100 Hg mm would have reasonably been considered desirable and within the normal range. The selections of both an optimal heart rate and systolic

pressure at which time the β_1-blocker should be administered are parameters well within the purview of the skilled cardiologist through no more than routine experimentation. It would have been reasonable to expect no patient would have been discharged from a hospital with congestive heart failure, third degree heart block or bronchospasm. Esmolol and atenolol are well established in the prior art as effective agents for reducing cardiovascular complications, as decreasing heart rate and blood pressure, following surgery. The continued administration of the β_1-adrenergic agent following surgery is conventional.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

July 1, 2002

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER